Journal of Science and Medicine in Sport 22 (2019) 1151–1156

Contents lists available at ScienceDirect

Journal of Science and Medicine in Sport

journal homepage: www.elsevier.com/locate/jsams

Original research

Vascular and oxygenation responses of local ischemia and systemic hypoxia during arm cycling repeated sprints

Sarah J. Willis[a,*], Arthur Peyrard[b], Thomas Rupp[b], Fabio Borrani[a,1], Grégoire P. Millet[a,1]

[a] Institute of Sport Sciences, Faculty of Biology and Medicine, University of Lausanne, Switzerland
[b] Laboratoire Interuniversitaire de Biologie de la Motricité (EA 7424 LIBM Chambéry), Université Savoie Mont Blanc, Campus Scientifique Technolac, France

ARTICLE INFO

Article history:
Received 27 March 2019
Received in revised form 26 April 2019
Accepted 7 May 2019
Available online 10 May 2019

Keywords:
Blood flow restriction
Occlusion
Perfusion
Extraction
Blood volume
Altitude

ABSTRACT

Objectives: The purpose of this study was to investigate the acute vascular and oxygenation responses to repeated sprint exercise during arm cycling with either blood flow restriction (BFR) or systemic hypoxia alone or in combination.
Design: The study design was a single-blinded repeated-measures assessment of four conditions with two levels of normobaric hypoxia (400 m and 3800 m) and two levels of BFR (0% and 45% of total occlusion).
Methods: Sixteen active participants (eleven men and five women; mean ± SD; 26.4 ± 4.0 years old; 73.8 ± 9.8 kg; 1.79 ± 0.07 m) completed 5 sessions (1 familiarization, 4 conditions). During each test visit, participants performed a repeated sprint arm cycling test to exhaustion (10 s maximal sprints with 20 s recovery until exhaustion) to measure power output, metabolic equivalents, blood flow, as well as oxygenation (near-infrared spectroscopy) of the biceps brachii muscle tissue.
Results: Repeated sprint performance was decreased with both BFR and systemic hypoxia conditions. Greater changes between minimum-maximum of sprints in total hemoglobin concentration (Δ[tHb]) were demonstrated with BFR (400 m, 45% and 3800 m, 45%) than without (400 m, 0% and 3800 m, 0%) ($p < 0.001$ for both). Additionally, delta tissue saturation index (ΔTSI) decreased more with both BFR conditions than without ($p < 0.001$ for both). The absolute maximum TSI was progressively reduced with both BFR and systemic hypoxia ($p < 0.001$).
Conclusions: By combining high-intensity, repeated sprint exercise with BFR and/or systemic hypoxia, there is a robust stimulus detected by increased changes in blood perfusion placed on specific vascular mechanisms, which were more prominent in BFR conditions.

Practical implications

- Though both conditions of BFR and systemic hypoxia impair repeated sprint performance, BFR requires different specific mechanisms than systemic hypoxia (vasodilation) to maintain oxygen delivery.
- By combining BFR and/or systemic hypoxia with high-intensity exercise, as repeated sprinting, there is a robust stimulus detected by increased changes in blood perfusion (Δ[tHb]) placed on the vascular mechanisms, which were more prominent in BFR conditions.
- We suggest these methods for possible incorporation within training programs, especially of the arms, to allow more efficient oxygen delivery via improved vascular conductance and therefore expect large performance improvement. However, further research with a training intervention is needed.

1. Introduction

In systemic hypoxic conditions where oxygen availability is limited and the demand for blood flow is magnified, a compensatory vasodilation occurs in order to increase oxygen delivery by way of greater blood flow to tissues.[1] When compared to systemic hypoxia, using blood flow restriction (BFR) that induces both ischemia and local hypoxia likely has a different effect on vascular/endothelial function due to specific vascular resistance and vessel diameter adjustment, accumulation of metabolites (nitric oxide, adenosine, prostaglandins, hydrogen ions, etc.) and/or sympathetic activation. In these BFR conditions of restricted vasodilation, the demand for increased blood flow cannot be meet with similar mechanisms. For example, a recent study with an acute

* Corresponding author at: Institute of Sport Sciences, Building Synathlon, Quarter UNIL-Centre, University of Lausanne, CH-1015, Lausanne, Switzerland.
E-mail address: sarah.willis@unil.ch (S.J. Willis).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jsams.2019.05.001
1440-2440/

repeated sprint leg cycling test to exhaustion found greater changes in tissue perfusion in blood flow restriction (BFR) conditions and thus suggested a possible stimulus for vascular regulation.[2] With high-intensity leg cycling exercise in systemic hypoxia (repeated sprint training in hypoxia, RSH), which has been shown to acutely reduce blood flow and vasodilation compared to normoxia,[3] training adaptation consists of greater perfusion in active muscles and improved vascular conductance.[4]

As modeled by di Prampero,[5] the determining factors of $V.O_{2max}$ and hemodynamic regulation are dependent on muscle mass. Muscles of small mass are characterized with different vascular properties than large mass muscles regarding the distribution of blood flow (difference in metabolic demand versus supply), smaller diffusing areas, and lower oxidative capacity, respectively.[6,7] Muscle properties including different phenotypes in the legs and arms are also involved with regulation of blood flow and pressure, as there are more myosin heavy chain type 2 fibers and larger type 2A fibers in arms than legs, which likely contributes to differing vascular function between limbs.[7] It is possible that muscles with small mass (arms) may be less impacted by the pressor reflexes,[8] therefore having a different impact on the regulation of vascular conductance[9] than legs. Interestingly, a threefold increase in variations in blood perfusion were found in the triceps brachii after six sessions in two weeks of RSH with the upper body (i.e. double poling),[10] whereas relatively smaller changes were observed in the vastus lateralis after eight sessions in four weeks of RSH (leg cycling).[4] Moreover, several authors have reported greater performance enhancement when RSH was performed with arms than with legs: cycling vs double poling in endurance athletes[4,10] or in elite rugby players.[11,12]

Therefore, the purpose of this study was to examine the vascular and oxygenation responses to acute repeated sprint arm cycling with conditions of systemic hypoxia, BFR, as well as in combination. It was hypothesized (1) that repeated sprint arm cycling performance would have greater performance impairment with systemic hypoxia, BFR, and the combination due to limited convective oxygen delivery and greater vascular resistance; (2) that greater changes in total hemoglobin would be elicited during sprints as the severity of systemic hypoxia and BFR increased; (3) that BFR alone and in combination with systemic hypoxia would elicit greater changes in total hemoglobin than systemic hypoxia alone due to different vascular mechanisms, which may decrease with duration of sprints due to fatigue and limited oxygen utilization near exhaustion.

2. Methods

There were 16 active participants involved in this study (eleven men and five women; mean ± SD; 26.4 ± 4.0 years old; 73.8 ± 9.8 kg; 1.79 ± 0.07 m). Participants trained ≥4 h/week including a variety of activities (running, cross-country skiing, swimming, climbing, cycling, resistance training), and were all accustomed to regular maximal intensity aerobic exercise. Individual informed consent was obtained after being informed of procedures and risks of the study. The protocol was approved by the Ethical Commission for Human Research (CER-VD 138/15) and performed within the seventh Declaration of Helsinki (2013). Participants were asked to avoid strenuous activity as well as caffeine or alcohol consumption 24 h before each visit. Further, all visits were standardized at the same time of day with at least 48 h between visits to limit fatigue.

Participants completed five sessions (one familiarization and four tests) of a randomized protocol assessing responses during a repeated sprint test to exhaustion (RST). The four testing conditions included normoxia (~400 m, F_IO_2 20.9%) and hypoxia (~3800 m normobaric hypoxia, F_IO_2 13.1 ± 0.1%), along with no BFR (0%) and BFR (45% of the pulse elimination pressure, detailed below). After critical assessment of number of sprints, power output, torque factor, pedaling frequency, and perceived effort during piloting sessions with arm cycling and RST, the percentage for BFR and resistance for arms were chosen.[2]

During familiarization, anthropometric data were measured and the informed consent and health questionnaire [Physical Activity Readiness Questionnaire, PAR-Q & YOU,[13] were completed. Participants donned the BFR cuff (custom-made 4 x 70 cm cuff, 3 × 41 bladder; D.E. Hokansson Inc., Bellevue, WA, USA) for measurement of the pulse elimination pressure (207 ± 28 mmHg). Pulse elimination pressure was measured at seated rest with the arm at approximately 60šof shoulder flexion with slight bend in the elbow by gradually inflating the cuff until the point at which no more arterial blood flow was detected via Doppler ultrasound (EchoWave II 3.4.4, Telemed Medical Systems, Telemed Ltd. Lithuania, Milano, Italy) of the brachial artery and was measured 2–3 times for accuracy, with ~2 min between trials.[14] Participants sat behind and slightly beneath a stand-mounted electronically-braked cycling ergometer (Lode Excalibur Sport Ergometer, Lode B.V., The Netherlands). The position was recorded and subsequently replicated. After a 5-min warm-up (1 W kg^{-1}), participants performed two 10 s maximal sprints with three minutes of active recovery between without BFR in order to both familiarize with the arm cycling ergometer and to warm up for the RST. After an additional 5-min passive recovery, participants were familiarized with the RST with no BFR, as described below. The "Wingate mode" of the ergometer was used for all sprints with an individually fixed torque factor (0.4 Nm kg^{-1}).

Each session began with a warm-up of 3 min at 30 W, 3 min at 60 W, followed by 6 min at 1 W kg^{-1} with a cadence of 85 rpm. After a brief recovery, two maximal 10 s warm-up sprints were performed (similar to familiarization). Oxygen uptake, heart rate, pulse oxygen saturation (SpO_2), and oxygenation (near-infrared spectroscopy, NIRS) were obtained throughout the RST. During BFR conditions, cuffs were placed bilaterally to the most proximal part of each arm and inflated 5 s before the RST remaining continuously inflated until the end of the post-RST measures (45% of pulse elimination pressure, 93 ± 12 mmHg). After a 1-min standardized rolling start (20 W, 85 rpm), participants began the RST of 10 s all-out maximal sprint and 20 s active recovery (20 W) (1:2 work-to-rest ratio) until exhaustion or task failure [cadence <70 rpm, similar to Ref. 4]. Participants were instructed to perform each sprint maximally and perform as many sprints as possible. Similar body position was maintained for all sprints and strong verbal encouragement was provided with no indication of the number of sprints performed. The first two sprints were carefully observed to be sure to reach ≥95% of the peak power from the best sprint from the two warm-up sprints in order to avoid pacing. Variables of mean power (mean of all sprints, W), number of sprints performed, and total work (kJ) were obtained. Following the completion of the test, blood flow (see details below), earlobe blood lactate concentration at 1-min post (Lactate Scout, EKF Diagnostics, GmbH, Leipzig, Germany), and rating of perceived exertion (RPE, Borg scale 6–20) were measured. The earlobe S_pO_2 was measured with an oximeter (8000Q2 Sensor, Nonin Medical Inc., Amsterdam, The Netherlands), one sample every 5 s, and reported as the lowest value of the final minute during the RST. Heart rate was monitored at 1 Hz with a telemetry-based heart rate monitor (Polar RS400, Kempele, Finland) to analyze the maximum value of all sprints.

With the left arm extended resting at ~80šhoulder flexion, Doppler blood flow was collected on the brachial artery in the day's condition (if BFR, cuffs inflated 1-min prior) with a linear probe (L12-5L60 N) using EchoWave II 3.4.4 software (Telemed Medical Systems, Telemed Ltd. Lithuania, Milano, Italy) ~5 min pre- and at

1-min post-RST. A 30 s video image was obtained and subsequent analysis was performed with post-RST to take an average of 10 frames, essentially a measurement every ~1.5 s. Blood flow was then calculated via a measurement of the vessel diameter (mm) and blood velocity (cm s^{-1}), along with shear rate [(mean velocity, cm s^{-1})/(diameter, mm)] to assess the rate which fluid or elastic lamina layers move past each other.

Breath-by-breath pulmonary gas-exchange was measured continuously throughout the exercise (Quark CPET, Rome, Italy). Oxygen consumption ($V.O_2$), ventilation ($V._E$), and respiratory exchange ratio (RER) were computed. The system was calibrated with a 3-L syringe (M9474, Medikro Oy, Finland) and a calibration was made with ambient air and known gas mixtures of O_2 (16%) and CO_2 (5%) prior to each measurement. During RST, the highest rolling 30 s average was obtained for oxygen uptake and the maximum values within those 30 s were analyzed for $V._E$ and RER.

NIRS measurements and analysis of peripheral oxygenation of the biceps brachii (PortaMonArtinis, Zetten, The Netherlands) were performed similarly as in Willis et al.[2] Signals were recorded at 10 Hz and exported (Oxysoft 3.0.53, Artinis, The Netherlands), and application of a 4th-order low-pass zero-phase Butterworth filter (cutoff frequency of 0.2 Hz) was used to reduce artifacts and smooth perturbations in the signal from pedaling strokes.[15] For each sprint, the maximum and minimum were detected automatically using the rapidly changing increase in deoxyhemoglobin as the visual parameter to confirm the starting point of the test. Identification of successive sprint and recovery phases was made and sprint phases were further analyzed. The change (Δ) in concentration for each sprint was then calculated as the difference between the detected maximum and minimum values for oxyhemoglobin ($\Delta[O_2Hb]$), deoxyhemoglobin (Δ[HHb]), total hemoglobin (Δ[tHb]), and tissue saturation index (ΔTSI, %). Absolute maximum TSI was obtained from each sprint. Data was normalized to the duration of the set; i.e. percentage of sprints performed (i.e., 20, 40, 60, 80, 100%), and a linear interpolation was used to calculate values when there was a fractional number of sprints, as each participant performed a different number of sprints in each condition.

After examining residual plots, no obvious deviations from homoscedasticity or normality were present. Linear mixed effects analyses were performed to evaluate oxygenation parameters regarding the relationship between fixed effects of condition (400 m, 0%; 400 m, 45%; 3800 m, 0%; 3800 m, 45%) and set duration (20, 40, 60, 80, 100% of sprints performed). Similarly, all other variables were analyzed with the fixed effect of condition. Participant was always set as the random effect. Analyses were performed using R (R Core team 2017, Foundation for Statistical Computing, Vienna, Austria) and nlme4.[16] The P values were set to 0.05 and obtained by likelihood ratio tests of the full model with the effect in question against the model without (control). To obtain contrasts, least-squares means for mixed models [library lsmeans,[17] using the Tukey method were computed. Values are represented as mean ± standard deviation. The magnitude of between-condition differences in the means were expressed as a standardized effect size (ES). Threshold values for effect size statistics were based on Cohen's d, where 0.2 is considered small, 0.5 medium, and 0.8 large.

3. Results

Table 1 illustrates the physiological responses of the arm-cycling RST. Number of sprints was lower in both hypoxic conditions (3800 m, 0% and 3800 m, 45%) compared with the control ($p < 0.001$; ES = 0.8 and 1.1). Mean power remained unchanged throughout all conditions ($p = 0.79$, NS). Total work decreased 23% between the control (400 m, 0%) and hypoxia alone (3800 m, 0%), as well as 53% between the control and 3800 m, 45% (both $p < 0.001$; ES = 0.9 and 1.2), which was an additional 39% decrease between 400 m, 45% and 3800 m, 45% ($p < 0.05$; ES = 1.0). Both SpO_2 and $V.O_2$ were decreased in both hypoxic (3800 m, 0% and 3800 m, 45%) than normoxic (400 m, 0% and 400 m, 45%) conditions (all $p < 0.001$; ES of SpO_2 all >2.4 and $V.O_2$ all >0.80). Further, maximal heart rate was lower in the combined (3800 m, 45%) than control condition ($p < 0.001$; ES = 0.3). Blood flow was 52% lower in 3800 m, 45% than 3800 m, 0% ($p < 0.05$; ES = 1.3) and 48% lower in 400 m, 45% than 3800 m, 0% ($p = 0.07$, trend; ES = 1.2). Systemic hypoxia (3800 m, 0%) demonstrated a greater shear rate (trend) compared to the BFR only condition (400 m, 45%; ES = 1.1; see Table 1).

No interactions were present for any oxygenation variables. As seen in Fig. 1, there were main effects of both condition and set duration with greater Δ[tHb] during both BFR conditions (400 m, 45% and 3800 m, 45%) than without (400 m, 0% and 3800 m, 0%) ($p < 0.001$ for both, Fig. 1B; ES range 0.5–0.7), and lower Δ[tHb] were seen near exhaustion ($p < 0.05$, Fig. 1A; ES range 0.3–0.5). Fig. 2 illustrates that absolute Δ[HHb] was greater in both 400 m, 45% ($p < 0.05$; ES = 0.3) and 3800 m, 45% ($p < 0.001$; ES = 0.4) than in hypoxia alone. Moreover, ΔTSI decreased with both BFR conditions than without ($p < 0.001$ for both; ES range 0.5–0.7); and that absolute maximum TSI decreased compared to the control and decreased in both hypoxic conditions compared to BFR alone ($p < 0.001$; ES range 0.6–1.9).

4. Discussion

The main findings indicated that (1) arm cycling performance is heavily impaired by systemic hypoxia conditions (number of sprints and total work) mainly due to decreased convective oxygen delivery (SpO_2, $V.O_2$); (2) both BFR alone and combined with systemic hypoxia elicited greater changes in total hemoglobin (Δ[tHb]) demonstrating valuable specific vascular responses compared to conditions without BFR; and (3) there was no additional effect of the combination of BFR and systemic hypoxia, when compared to BFR alone.

Generally, exercise requires augmentation of blood flow and thereby increased laminar shear stress, both which are responsible for metabolic upregulation of endothelial nitric oxide synthase[18,19] and may improve flow-mediated dilation.[20] This response is proportional to exercise intensity and therefore, the demand should increase with high-intensity exercise (such as repeated sprint performance) as previously suggested.[1,21] In addition, similar vasodilation mechanisms during conditions of systemic hypoxia exist but to a greater extent due to reduced oxygen availability.[1] Though differences were not significant between the control (400 m, 0%) and other conditions, the present study suggests greater shear stress during systemic hypoxia (3800 m, 0%) compared to the BFR only condition (400 m, 45%; trend, ES = 1.1; see Table 1).

As expected, there was impaired arm cycling performance with systemic hypoxia likely due to limited oxygen delivery, thus lower number of sprints and total work. Though this study is unable to confirm the vasodilation that generally occurs in systemic hypoxia situations, the results can suggest that hypoxia-induced vasodilation increases blood volume as a way to increase blood flow to provide more oxygen and allow greater oxygen utilization (increased extraction and thus lower changes in [HHb], Fig. 2), which possibly limits oxygen delivery (lower SpO_2 and $V.O_2$). Similar interpretation has been previously suggested such that lower changes in [HHb] demonstrated possible near-maximal peripheral deoxygenation.[22] This was not the case in BFR conditions, as there was decreased post blood flow (and hence shear rate, Table 1) to tissues by the partial occlusion and thus higher vascular resistance. Therefore, BFR (local ischemia) elicits different vasodilatory responses than systemic hypoxia conditions. In fact, BFR blunts

Table 1
Average physiological responses of the arm-cycling repeated sprint test to exhaustion in conditions of normoxia (400 m) and normobaric hypoxia (3800 m) combined with blood flow restriction (0% and 45%).

	400 m 0%	400 m 45 %	3800 m 0%	3800 m 45%
Number of sprints	12 ± 8	9 ± 5	7 ± 3 ***	6 ± 1 ***
Mean power (W)	353 ± 111	343 ± 104	337 ± 120	339 ± 110
Total work (kJ)	40 ± 25	30 ± 16	23 ± 12 ***	19 ± 6 ***, #
SpO_2 (%)	95.9 ± 2.7	95.5 ± 3.3	85.9 ± 3.5 ***, ###	87.8 ± 3.1 ***, ###, &
Maximal heart rate (bpm)	174 ± 12	173 ± 13	173 ± 11	171 ± 10 ***
Blood lactate (mmol L^{-1})	10.4 ± 2.9	11.0 ± 3.6	10.8 ± 3.3	10.3 ± 3.7
RPE arms (Borg 6–20)	17.9 ± 1.6	18.4 ± 1.5	18.1 ± 1.8	18.7 ± 1.3
RPE breathing (Borg 6–20)	16.2 ± 2.1	16.0 ± 2.2	16.8 ± 2.7	16.2 ± 2.3
$V.O_2$ (mL min^{-1} kg^{-1})	43.1 ± 6.7	43.4 ± 7.7	38.2 ± 5.5 ***,###	37.5 ± 6.2 ***,###
$V_{.E}$ (L min^{-1})	146 ± 29	148 ± 24	151 ± 30	152 ± 23
RER	1.01 ± 0.06	1.03 ± 0.08	1.02 ± 0.07	1.02 ± 0.09
Post-blood flow (mL min^{-1})	605 ± 549	408 ± 307	779 ± 318 (# *trend*)	377 ± 309 &
Post-diameter (mm)	4.7 ± 0.4	4.5 ± 0.7	4.7 ± 0.4	4.4 ± 0.6
Post-shear rate (s^{-1})	131 ± 112	95 ± 63	163 ± 62 (# *trend*)	93 ± 68

Mean ± SD.
*** ($p < 0.001$) significantly different than 400 m, 0%.
($p<0.001$), # ($p<0.05$) significantly different than 400 m, 45%.
&& ($p<0.01$), & ($p < 0.05$) significantly different than 3800 m, 0%.
SpO_2, pulse oxygen saturation; RPE, rating of perceived exertion; $V.O_2$, oxygen consumption; $V_{.E}$, minute ventilation; RER, respiratory exchange ratio.

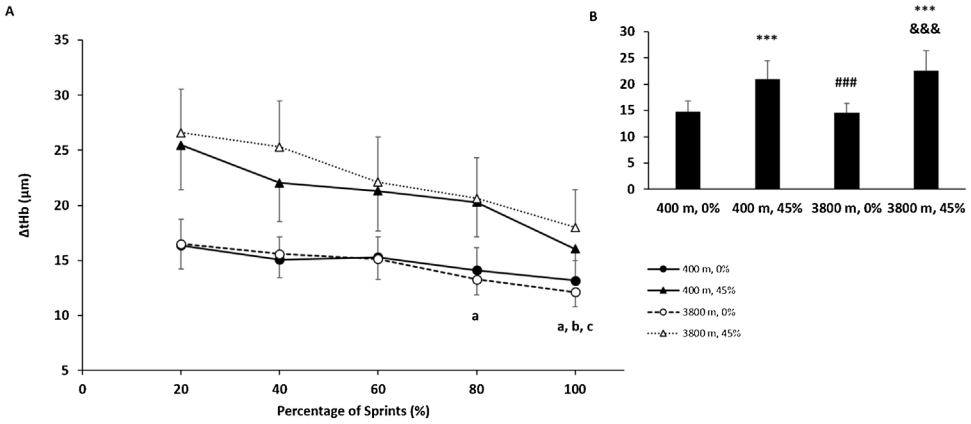

Fig. 1. Representation of near-infrared spectroscopy (NIRS) based oxygenation response of the average maximum-minimum delta (Δ) concentration of total hemoglobin ([tHb]) of each sprint for the biceps brachii during the repeated sprint test to exhaustion in (A) percentage of sprints performed, (B) across conditions of blood flow restriction and systemic hypoxia.
Mean ± SE. *** ($p < 0.001$) significantly different than 400 m, 0%; ### ($p<0.001$) significantly different than 400 m, 45%; &&& ($p < 0.001$) significantly different than 3800 m, 0%; a ($p < 0.05$) significantly different than 20%; b ($p < 0.05$) significantly different than 40%; c ($p < 0.05$) significantly different than 60%.

the effect of hypoxia-induced vasodilation, even though combined with high-intensity, as shown by the decreased blood flow and oxygenation responses of the combined BFR and systemic hypoxia condition (3800 m, 45%).

With both BFR conditions (400 m, 45% and 3800 m, 45%) in the present study, greater changes in [tHb] (blood volume[23]) were demonstrated during the RST (Fig. 1). As well, Δ[tHb] across all conditions were lower near exhaustion (Fig. 1). Prior training studies performing repeated sprints in hypoxia have eluded to increased variation in perfusion during both leg cycling[4] and double poling.[10] Similar research has shown this response during acute leg cycling RST with different levels of BFR,[2] as well as after 6 weeks of single-leg cycling with BFR performing 3 sets of 3 × 2 min interval training,[24] and additionally with 4 weeks of single-leg knee extension with BFR.[25] The present arm cycling result was therefore expected.

As there was lower blood flow in both BFR conditions compared with systemic hypoxia alone (Table 1), these conditions trigger different compensatory mechanisms to limit this alteration in blood flow and oxygen delivery to tissue: beyond the reported increase in blood volume variation (and probable greater changes in blood pressure via increased preload, stroke volume, and cardiac output) during sprints with both BFR conditions, there are likely other mechanisms with neural (blunt vasoconstriction, or induce sympathetic cholinergic vasodilation), metabolic (increased metabolite accumulation, nitric oxide synthesis), and mechanical (muscle and respiratory pump, increased arterio-venous pressure gradient – perfusion pressure; vascular enlargement)[1] influences, all being regulated by blood pressure and muscle oxygen consumption.[26] Further, Mortensen et al.[21] proposed that while cardiac output and local muscle vessel vasoconstriction are major limiting factors of muscle blood flow during high-intensity exercise, perfusion pressure is not. This allows the continual consideration of the pressure gradient as a probable mechanism for such increased changes in blood volume during the present study. Additionally, it has been suggested that pressor reflexes may play less of a role in exercise involving smaller muscle mass (arms vs legs),[8] however the muscle metaboreflex is triggered with accumulation of metabolites and reduced oxygen availability.[27] Further, it is unknown about the degree to which differences in muscle phenotypes of the legs and arms can contribute to the hemodynamics and influence the pressor reflexes. The changes in TSI during repeated sprints of the current study were lower in both BFR conditions (Fig. 2) due to overall lower TSI at the start due to partial occlusion. However,

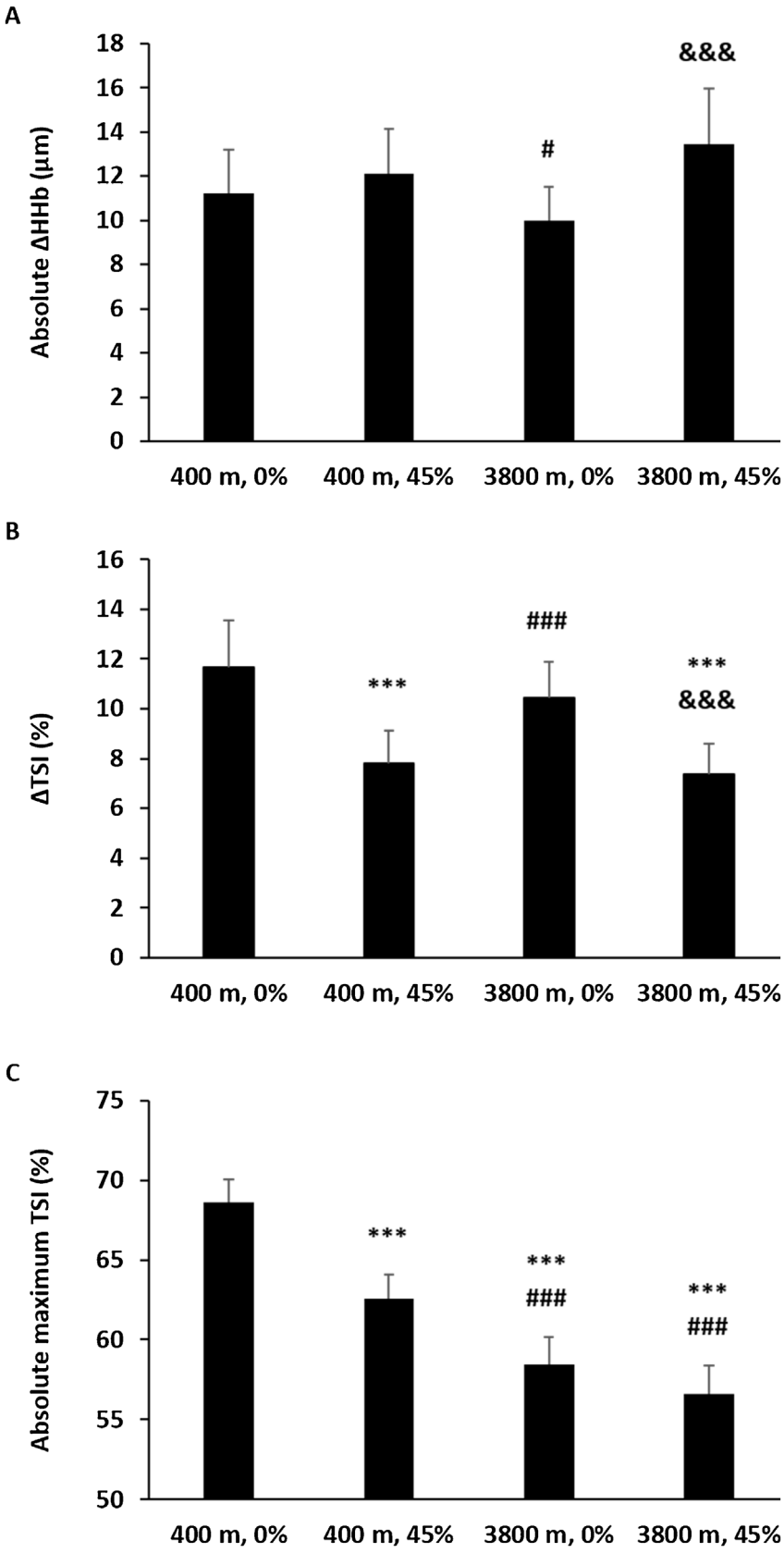

Fig. 2. Near-infrared spectroscopy (NIRS) representation of the average maximum-minimum delta (Δ) responses of each sprint for the biceps brachii during the repeated sprint test to exhaustion in (A) absolute Δ [HHb], (B) Δ tissue saturation index (TSI), and (C) absolute maximum TSI, across conditions of blood flow restriction and systemic hypoxia.
Mean ± SE. *** ($p < 0.001$) significantly different than 400 m, 0%; ### ($p < 0.001$), # ($p<0.05$) significantly different than 400 m, 45%; &&& ($p < 0.001$) significantly different than 3800 m, 0%.

this could also indicate that the external pressure of these conditions increased oxygen extraction and may reach closer to maximal capacity than compared with hypoxia alone. Together, stimulation of the muscle metaboreflex is quite likely in these unique conditions, even in the arms, thus warranting further research.

As previous research has demonstrated, these hypoxia and BFR conditions induce large increases in deoxygenation of the legs (probably due to a large amount of active muscle mass).[2,22] Additionally, it has been shown that legs are quite responsive (greater changes in perfusion) during systemic hypoxia[22] and BFR conditions,[2] as is substantially confirmed to a greater extent in the present study of the arms. Collectively, this demonstrates that there are differing vascular properties and responses between limbs.

5. Conclusion

The present study combining acute repeated-sprint exercise with BFR and/or systemic hypoxia during arm cycling demonstrated greater changes in blood perfusion with both BFR alone and in combination with systemic hypoxia. In systemic hypoxia, these variations in perfusion are likely derived from compensatory vasodilation. Whereas, perfusion changes in BFR conditions may result from the stimulation of several specific mechanisms (such as perfusion pressure, pressor reflexes) to restore oxygen delivery, since BFR increases vascular resistance and restricts vasodilation. We suggest that the intrinsic vasodilatory response was likely different in both acute BFR conditions compared to the other conditions with no BFR. The current results confirm a profound vascular stimulus in the small muscle mass exercise of arm cycling when combining repeated sprint exercise with both BFR and systemic hypoxia alone and in combination, which were more pronounced in BFR conditions.

Acknowledgements

The authors would like to thank the participants for their efforts, time commitment, and cooperation with this study. There has been no financial assistance given with this project.

References

1. Casey DP, Joyner MJ. Compensatory vasodilatation during hypoxic exercise: mechanisms responsible for matching oxygen supply to demand. *J Physiol* 2012; 590(24):6321–6326.
2. Willis SJ, Alvarez L, Borrani F et al. Oxygenation time course and neuromuscular fatigue during repeated cycling sprints with bilateral blood flow restriction. *Physiol Rep* 2018; 6(19):e13872.
3. Calbet JA. Oxygen tension and content in the regulation of limb blood flow. *Acta Physiol Scand* 2000; 168(4):465–472.
4. Faiss R, Leger B, Vesin JM et al. Significant molecular and systemic adaptations after repeated sprint training in hypoxia. *PloS One* 2013; 8(2):e56522.
5. di Prampero PE. Factors limiting maximal performance in humans. *Eur J Appl Physiol* 2003; 90(3-4):420–429.
6. Calbet JA, Holmberg HC, Rosdahl H et al. Why do arms extract less oxygen than legs during exercise? *Am J Physiol Reg Integr Comp Physiol* 2005; 289(5):R1448–R1458.
7. Ortenblad N, Nielsen J, Boushel R et al. The muscle fiber profiles, mitochondrial content, and enzyme activities of the exceptionally well-trained arm and leg muscles of elite cross-country skiers. *Front Physiol* 2018; 9:1031.
8. Volianitis S, Yoshiga CC, Vogelsang T et al. Arterial blood pressure and carotid baroreflex function during arm and combined arm and leg exercise in humans. *Acta Physiol Scand* 2004; 181(3):289–295.
9. Holmberg HC. The elite cross-country skier provides unique insights into human exercise physiology. *Scand J Med Sci Sports* 2015; 25(Suppl 4):100–109.
10. Faiss R, Willis S, Born DP et al. Repeated Double-Poling Sprint Training in Hypoxia by Competitive Cross-country Skiers. *Med Sci Sports Exerc* 2014; 47(4):809–817.
11. Beard A, Ashby J, Chambers R, Brocherie F, Millet GP. Repeated-Sprint Training in Hypoxia in International Rugby Union Players. *Int J Sport Physiol Perform* 2018:1–15.
12. Beard A, Ashby J, Kilgallon M, Brocherie F, Millet GP. Upper-body repeated-sprint training in hypoxia in international rugby union players. *Eur J Sport Sci* 2019:1–9.
13. Physiology CSfE. PAR-Q & YOU. 2002.
14. Gualano B, Ugrinowitsch C, Neves Jr M et al. Vascular occlusion training for inclusion body myositis: a novel therapeutic approach. *J Vis Exp* 2010;(40).
15. Rodriguez RF, Townsend NE, Aughey RJ et al. Influence of averaging method on muscle deoxygenation interpretation during repeated-sprint exercise. *Scand J Med Sci Sports* 2018; 28(11):2263–2271.
16. Pinheiro J. BD, DebRoy S., Sarkar D., and R Core Team nlme: Linear and Nonlinear Mixed Effects Models. https://CRAN.R-project.org/package=nlme.
17. Lenth RV. Least-squares means: the R package lsmeans. *J Stat Softw* 2016; 69(1):33.
18. Gielen S, Schuler G, Hambrecht R. Exercise training in coronary artery disease and coronary vasomotion. *Circulation* 2001; 103(1):E1–E6.
19. Tinken TM, Thijssen DH, Hopkins N et al. Impact of shear rate modulation on vascular function in humans. *Hypertension* 2009; 54(2):278–285.
20. Katayama K, Fujita O, Iemitsu M et al. The effect of acute exercise in hypoxia on flow-mediated vasodilation. *Eur J Appl Physiol* 2013; 113(2):349–357.
21. Mortensen SP, Damsgaard R, Dawson EA, Secher NH, Gonzalez-Alonso J. Restrictions in systemic and locomotor skeletal muscle perfusion, oxygen supply and VO_2 during high-intensity whole-body exercise in humans. *J Physiol* 2008; 586(10):2621–2635.
22. Willis SJ, Alvarez L, Millet GP, Borrani F. Changes in muscle and cerebral deoxygenation and perfusion during repeated sprints in hypoxia to exhaustion. *Front Physiol* 2017; 8:846.
23. Van Beekvelt MC, Colier WN, Wevers RA, Van Engelen BG. Performance of near-infrared spectroscopy in measuring local O(2) consumption and blood flow in skeletal muscle. *J Appl Physiol (1985)* 2001; 90(2):511–519.
24. Christiansen D, Eibye KH, Rasmussen V et al. Cycling with blood flow restriction improves performance and muscle K(+) regulation and alters the effect of antioxidant infusion in humans. *J Physiol* 2019; 597(9):2421–2444.
25. Kacin A, Strazar K. Frequent low-load ischemic resistance exercise to failure enhances muscle oxygen delivery and endurance capacity. *Scand J Med Sci Sports* 2011; 21(6):E231–E241.
26. Corvino RB, Rossiter HB, Loch T, Martins JC, Caputo F. Physiological responses to interval endurance exercise at different levels of blood flow restriction. *Eur J Appl Physiol* 2017; 117(1):39–52.
27. Kaufman MP, Hayes SG. The exercise pressor reflex. *Clin Auton Res* 2002; 12(6):429–439.